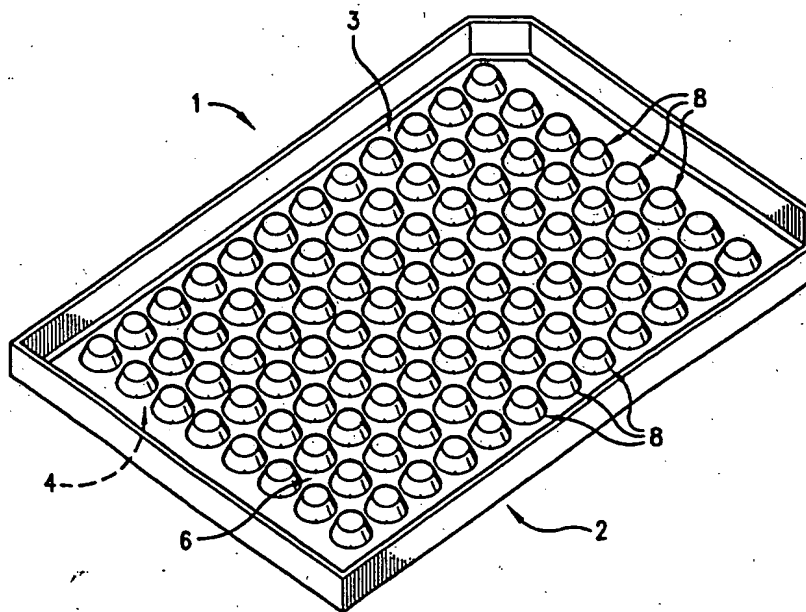


(51) International Patent Classification ⁶ : B01L 3/00, G01N 31/00	A1	(11) International Publication Number: WO 99/44742 (43) International Publication Date: 10 September 1999 (10.09.99)
<p>(21) International Application Number: PCT/US99/04454</p> <p>(22) International Filing Date: 1 March 1999 (01.03.99)</p> <p>(30) Priority Data: 60/076,581 3 March 1998 (03.03.98) US 9813578.3 24 June 1998 (24.06.98) GB</p> <p>(71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).</p> <p>(72) Inventor; and (75) Inventor/Applicant (for US only): FEIGLIN, Marc [AU/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).</p> <p>(74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).</p>	<p>(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p>	

(54) Title: SEALING APPARATUS FOR USE WITH MICROPLATES



(57) Abstract

The present invention relates to a sealing apparatus (1) that effectively seals microplates and can be used in conjunction with automated equipment. While the present invention is adaptable to automated instruments, it does not require sophisticated machinery to utilize the apparatus.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China	KZ	Kazakhstan	PT	Portugal		
CU	Cuba	LC	Saint Lucia	RO	Romania		
CZ	Czech Republic	LI	Liechtenstein	RU	Russian Federation		
DE	Germany	LK	Sri Lanka	SD	Sudan		
DK	Denmark	LR	Liberia	SE	Sweden		
EE	Estonia			SG	Singapore		

TITLE OF THE INVENTION
SEALING APPARATUS FOR USE WITH MICROPLATES

BACKGROUND OF THE INVENTION

5 Modern diagnostic medicine depends on the routine testing of biological samples from sources such as blood, serum, spinal fluid, urine, tissue specimens, etc. In addition, many other industries and research facilities run both chemical and biological tests in large numbers. In order to perform the running of large numbers of tests
10 efficiently, accurately, and safely, the "hardware" used in the performance of the tests can be of critical importance.

 Microtiter plates or "microplates" were introduced in the 1960's to facilitate laboratory testing in situations where a large number of tests were run simultaneously. Microplates come in various sizes,
15 from 6 to 9600 wells. The most typical microplates contain ninety-six (96) molded plastic wells (in an 8 x 12 array) with a typical sample volume capacity of about 200 microliters. A wide variety of mechanical fluid handling devices are now available so that specimens, chemical solutions and other liquids can be transferred into the wells. Usually a
20 row of eight (8) or twelve (12) wells are filled simultaneously, but some handling devices can simultaneously add sample to all of the wells. The lids of the microplates are designed to prevent dust or other contaminants from entering the wells, as well as to slow down the rate of evaporation. Usually the lids are sturdy enough so that they can be
25 removed and placed on the microplates by a variety of automated scientific instruments and robotic arms.

 The design of the microplate is less than optimal in several ways. Most microplates have loose fitting lids, which are not designed to seal the top of the open wells of the microplates. As a consequence,
30 liquid can spill out of the well or aerosols can form during filling. This can ruin the test and may also create a hazard if the testing involves infectious material.

 Because the lids do not create a tight seal there is a tendency for condensation to form from the wells. Over time, this condensation
35 can spread along the lid creating cross-contamination between the

samples in the wells. Sealing mats are available that can be used to seal the microplates. The mats are often made of polypropylene or silicone. Such materials create sealing mats that are too thin to be handled by most automated instruments. The polypropylene mats require
5 significant pressure to place and remove them, and the silicone mats are too flimsy for a machine to maneuver them.

It is the object of this invention to provide an inexpensive, easily manufactured sealing apparatus used in conjunction with microplates that is easily adaptable for use by automated instruments.

10

SUMMARY OF THE INVENTION

The present invention relates to a sealing apparatus that effectively seal microplates and can be used in conjunction with automated equipment. While the present invention is adaptable to
15 automated instruments, it does not require sophisticated machinery to utilize the apparatus. The types of device which would be capable of manipulating the instant invention include, but are not limited to, laboratory robot arms, such as those from Beckman, CRS Robotics, Mitsubishi Robotics and Zymark. Specific types of laboratory robot arms
20 include, but are not limited to, Tecan Genesis RMP, Rosys Plato 2000 and Beckman Biomek.

The invention relates to a sealing apparatus comprising:
a lid which is designed to be used with microplates, having
an outer surface and an inner surface; and
25 a microplate mat having a top side and a bottom side, the bottom side having multiple protrusions formed thereon which correspond to and seal an array of openings in a microplate, the top side of the microplate mat being attached to the inner surface of the lid.

Still other objects and advantages of the present invention
30 will become readily apparent to those skilled in this art from the following detailed description, wherein only the preferred embodiment of the invention has been shown, simply by way of illustration of the best mode contemplated. As will be realized, the invention is capable of modifications in various aspects, all without departing from the

invention. Accordingly, the drawings and description are to be regarded as illustrative in nature, and not as restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

5 The present invention may be described with greater clarity and specifically with reference to the drawings, in which:

Figure 1 is a view in perspective of the preferred embodiment of the invention;

10 Figure 2 is a view in perspective of the microplate mat; and
Figure 3 is a view in perspective of the microplate lid.

DETAILED DESCRIPTION OF THE INVENTION

Referring more particularly to the drawings, wherein like numbers designate like parts throughout, FIG. 1 represents the invention, as assembled, in two dimensions. The sealing apparatus (1) comprises a lid (2) and a microplate mat (3). As shown in FIG. 3, the lid (2) has an outer surface (4) and an inner surface (5). The lid (2) is made from a rigid material. Examples of such rigid materials include, but are not limited to, polystyrene, polypropylene, polycarbonate or acrylic.

20 As shown in FIG. 2, the microplate mat (3) has a top side (6) and a bottom side (7). Multiple protrusions (8) are formed on the bottom side (7) of the microplate mat (3). These protrusions (8) correspond to and seal an array of openings found in a microplate. The number of protrusions (8) formed on the mat (3) can vary, depending on the size of the microplate being used. Typically, most mats (3) will contain 6 to 384 protrusions (8). Of course, the number of protrusions will depend on the microplate used and the number of wells in the microplate. The top side (6) of the microplate mat (3) is attached to the inner surface (5) of the lid (2). The microplate mat (3) is made from a flexible material.

25 Examples of such flexible materials include, but are not limited to, silicone, polypropylene, sodium polysulfide, polychloroprene (neoprene), butadienestyrene copolymers (SBR), rubber and the like.

30 The microplate mat (3) is attached to the inner surface (5) of the lid (2) by using a solvent resistant adhesive appropriate for the

materials being joined. Types of solvent resistant adhesives include, but are not limited to, glue or double-sided adhesive tape. Other methods for attaching the microplate mat and the lid, such as molding, heating and other techniques known in the art, may also be used.

5 In operation, the sealing apparatus (1) is placed on top of a microplate by an automated instrument so that the protrusions (8) sit in the openings of the microplate. When the automated instrument applies the necessary pressure, the protrusions (8) seal the openings of
10 microplate and prevent evaporation or cross-contamination. In a similar manner, the sealing apparatus (1) can be removed from the microplate by a simple lifting action of an automated instrument.

15 In this disclosure, there is shown and described only the preferred embodiment of the invention, but, as aforementioned, it is to be understood that the invention is capable of changes or modifications within the scope of the inventive concept as expressed herein.

WHAT IS CLAIMED IS:

1. A sealing apparatus comprising:
a lid which is designed to be used with microplates, having
5 an outer surface; and an inner surface; and

a microplate mat having a top side and a bottom side, the
bottom side having multiple protrusions formed thereon which
correspond to and seal an array of openings in a microplate, the top side
10 of the microplate mat being attached to the inner surface of the lid.

2. The sealing apparatus of Claim 1 wherein the lid is
made of non-flexible material comprising polystyrene, polypropylene,
polycarbonate or acrylic.
15

3. The sealing apparatus of Claim 2 wherein the mat is
made of flexible material comprising silicone, polypropylene, sodium
polysulfide, polychloroprene (neoprene), butadienestyrene copolymners
(SBR), or rubber.
20

4. The sealing apparatus of Claim 3 wherein the mat is
attached to the lid with an adhesive comprising glue or double-sided
adhesive tape.



1/3

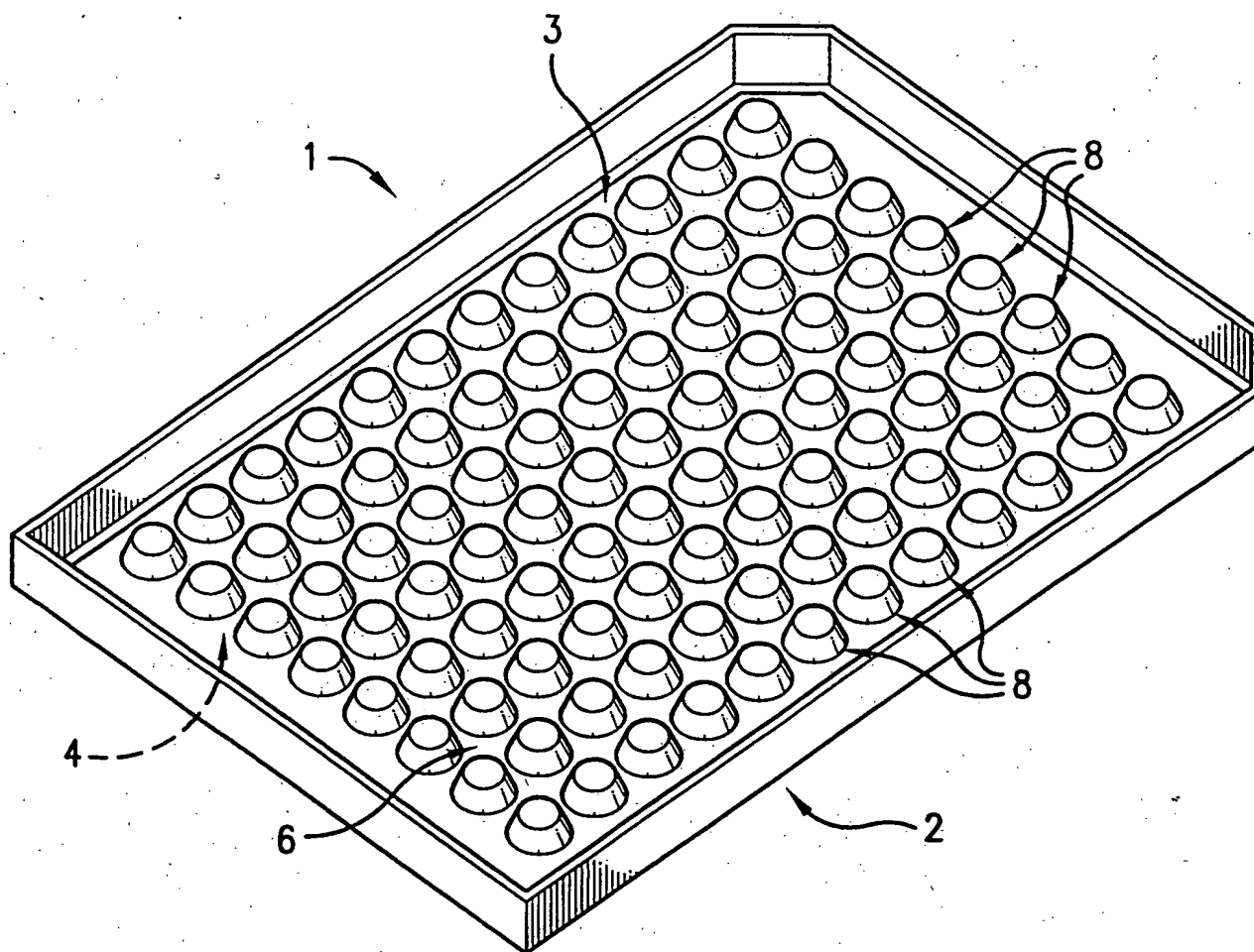


FIG. 1

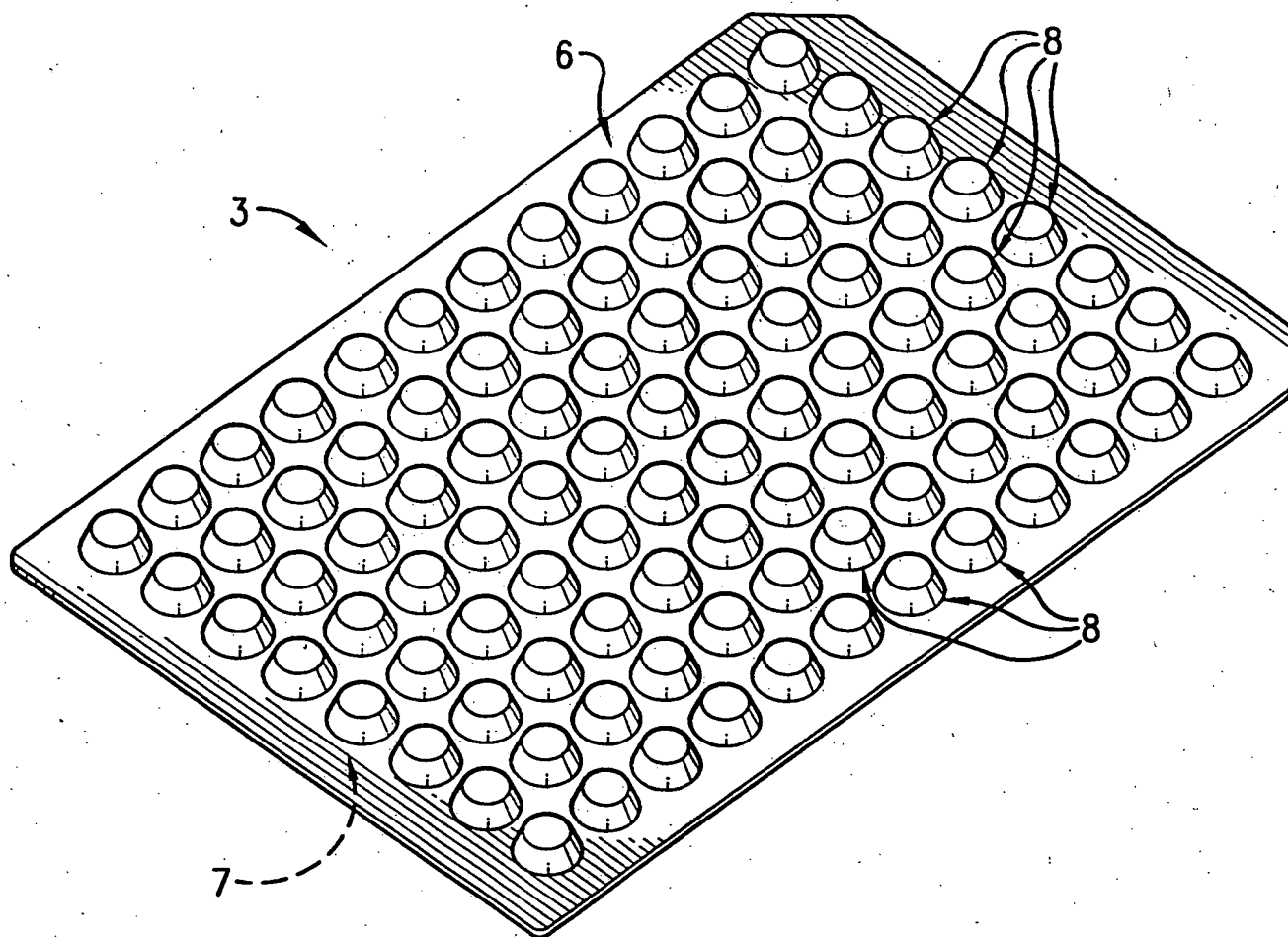


FIG. 2

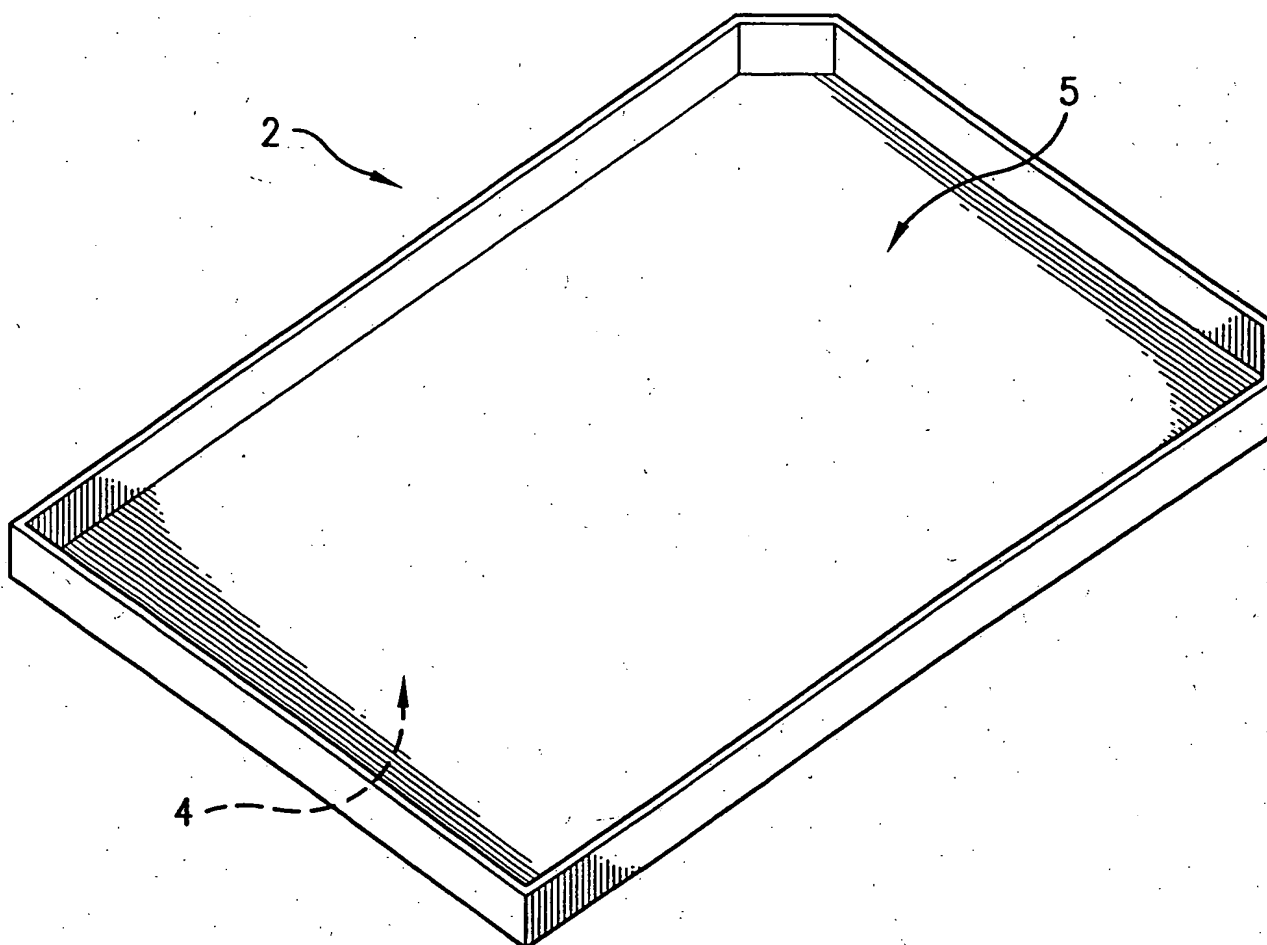


FIG.3

INTERNATIONAL SEARCH REPORT

International application No.
T/US99/04454

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :B01L 3/00; G01N 31/00
US CL :422/102,58; 436/809; 435/33
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/102, 58; 436/809, 535, 823; 435/33, 288.5, 305.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS search terms: (microplate# or micro(la)plate# or microtiter or microtitre), protrusions, polystyrene, polypropylene, polycarbonate, acrylic, tape, adhesive, glue.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,780,285 A (KUYPERS et al) 25 October 1988 (25-10-88), claims 6-9, col. 6, lines 22-27.	1, 3
Y	US 5,618,701 A (LANDEGREN) 08 April 1997 (08-04-97), col. 7, lines 48-50.	2, 4
A	US 4,077,845 A (JOHNSON) 07 March 1978 (07-03-78).	1-4
A	US 5,346,672 A (STAPLETON et al) 13 September 1994 (13-09-94).	1-4
A	US 5,665,247 A (VALUS et al) 09 September 1997 (09-09-97).	1-4
A	US 5,721,136 A (FINNEY et al) 24 February 1998 (24-02-98).	1-4
A,P	US 5,759,784 A (ASP et al) 02 June 1998 (02-06-98).	1-4

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

Special categories of cited documents:		*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A	document defining the general state of the art which is not considered to be of particular relevance	*X	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B	earlier document published on or after the international filing date	*Y	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A	document member of the same patent family
*O	document referring to an oral disclosure, use, exhibition or other means		
*P	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

07 MAY 1999

Date of mailing of the international search report

26 MAY 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

Kevin P. Cannell

Telephone No. (303) 308-0661

